

## 'Keep at It! Accept the Challenges of Your Critics'

An Interview with John M. Howard, MD, Professor Emeritus, Division of General Surgery, University of Toledo, Toledo, Ohio, USA

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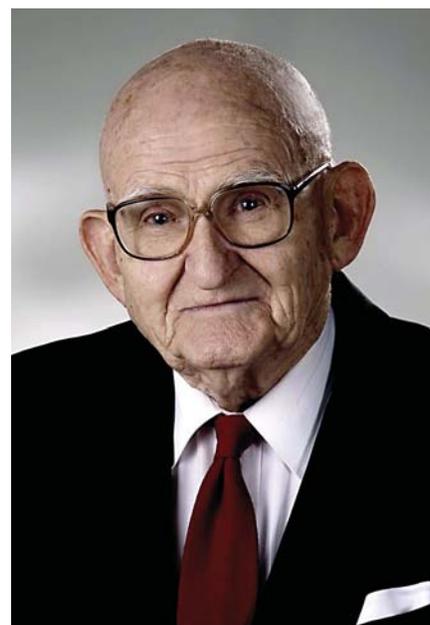
### Abstract

In this article, Professor John Howard shares with our readers his life experiences as a pancreatic surgeon-researcher and gives advice to junior pancreatologists starting a career in pancreatic research. Professor Howard made an outstanding contribution to the understanding of acute pancreatitis and he is a pioneer in the development of management approaches for pancreatic diseases.

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**M.E.F.-Z.:** What initiated you to work in pancreatic research in the first place?

**J.M.H.:** It was 1942. As a sophomore student in the University of Pennsylvania School of Medicine, I was studying Pathology. Ralph Jones, a senior student, suggested that I study the anatomy of the pancreatic ampulla. 'Is reflux of bile into the pancreatic ducts anatomically possible?' Dr. William Ehrich, Professor of Pathology at Penn, was a refugee from Germany and Chairman of the Department of Pathology at the adjacent Philadelphia General Hospital. He was a wonderful teacher whose support was generously provided. 'You may dissect the pancreas from each of the autopsies performed here on Sundays', he said, 'providing that you point out any evidence of disease identified'. Of 150 dissections 'a common channel' was found in 'at least 50%' (a confirmatory finding).



*Prof. John M. Howard*

Before publication the paper was presented on Student Research Day at the university. The distinguished Visiting Pathologist, Professor Milton C. Winternitz of Yale, in his concluding address, commented that the: 'Anatomy of the pancreatic duct might not be the most important

**Table 1.** Acute pancreatitis (1922–1946 inclusive), Hospital of the University of Pennsylvania

Diagnosis	Number of patients	Mortality rate
Acute pancreatitis	80	29%
Hemorrhagic pancreatitis	21	76%
Edematous pancreatitis	59	12%
Edema – no fat necrosis	28	7%
Edema – with fat necrosis	31	15%

topic for research, but it might get a fellow interested and over a career he might make a major contribution.’ As I well recall, it was wartime and there had been only five papers. Four prizes had traditionally been presented. My paper had tied for 4th prize! But Dr. Winternitz was right: interest is proving lifelong.

**M.E.F.-Z.:** You have pioneered pancreatic research in so many directions. At the end of the day what has given you the most satisfaction?

**J.M.H.:** Two findings:

*The first:* Acute pancreatitis is not a disease. It consists of (or is an expression of) multiple diseases. In our early days, pancreatitis was considered by most clinicians to be a single disease. Of course this isn’t true. Like pneumonia or gastroenteritis it consists of many diseases.

In 1946 the youthful author, with the support of his surgical mentor, Dr. I.S. Ravdin, reviewed the records of all 80 patients with acute pancreatitis who had been admitted to the University of Pennsylvania Hospital in the previous 25 years (1922–1946 inclusive). The hospital mortality rate had been about 30%. The diagnosis on each patient had been made at laparotomy or autopsy. Each patient had been given the unmodified diagnosis, acute pancreatitis. Although not so classified, all were idiopathic in that era. Fifty-three (two thirds) of the patients had had gallstones, but pancreatitis had not been attributed to the gallstones. Furthermore, of those patients having undergone laparotomy, the majority had had a cholecystostomy regardless of the presence or absence of gallstones.

Accepting the then current concept that all acute pancreatitis was idiopathic, the patients were given a pathologic diagnosis based on gross description of the pancreas. The findings are shown in table 1.

Later, Dr. George Jordan, Jr. and I were young surgical colleagues at Baylor University in Houston. Dr. Jordan was working primarily in the Veterans Administration

Hospital and I was working across town in the Jefferson Davis (Charity) Hospital. In systematically reviewing our pancreatitis patients, the alcoholic patients at the VA were found to have quite a different disease from those nonalcoholic patients at the Charity Hospital. The analysis was extended and I presented the data at a Pan-Pacific Surgical Association Meeting in Honolulu. A most distinguished surgeon was chairing the session of a hundred or more surgeons and, in opening the discussion of my paper, he expressed the thought that alcohol and alcoholism had little or no relationship to pancreatitis. His patients and our patients were culturally and economically miles apart! As the observations expanded and the principle became fully established, scores, perhaps hundreds of observers contributed. Acute pancreatitis was not a disease. It was clearly a reflection of multiple diseases, perhaps of a hundred or more! Each differed in its etiology, natural history and essential treatment.

*The second finding:* Before 1968, around the world, the mortality rate of the Whipple resection of the head of the pancreas had been approximately 25%. The leader of a major American clinic wrote that the mortality rate was so high that he would henceforth perform only bypass operations.

In that year, 1968, I reported 41 consecutive resections of the head of the pancreas without an intervening death. At that time this had been a very significant achievement. Success had been due to gradual improvements in the details of operation as tested in the operating room of both the hospital and the animal laboratory, by increasing attention to pre- and postoperative care and by teamwork between doctors, intensive care nurses, residents and anesthesiologists. The management of each patient was carefully reviewed before and after operation. Was this research? You bet it was! After several of the resections, as surgeon, I had slept in the Surgical Intensive Care Unit for the first one or two postoperative nights in order to determine adequate fluid replacement. To reiterate: was this research? Yes, the environment of the operating room can be a laboratory in the finest sense of the term. Subsequently, I modified an operative technique that has resulted in making the often fatal postoperative pancreatojejunal fistula a preventable complication. In their careers, of course, Dr. Kenneth Warren, Dr. William Longmire, Dr. Hans Beger and others have made significant contributions to these advances. Today, around much of the world, the duplication of these findings is gradually leading to the establishment of centers of excellence for the treatment of pancreatic disease.

**M.E.F.-Z.:** Based on your experience as mentee and mentor can you comment on the value of mentorship for the development of a new investigator?

**J.M.H.:** There was relatively limited interest in the pancreas among surgeons when the writer's career began in the 1940s. But in 1921 Charles H. Best, the medical student, had had a wonderful mentor in the surgeon, Dr. Frederick Banting, when they jointly discovered insulin. The value of mentorship for the youthful investigator would have been more widely recognized (a point on which his mentor unsuccessfully insisted), if Best, the co-investigator, had shared the Nobel Prize with his mentor. The original idea had been that of the mentor who had stimulated and, who subsequently led, the younger investigator to becoming Professor and Chairman of the Department of Physiology at the University of Toronto at age 29.

Paul Langerhans, Jr. and his mentor, Professor Rudolph Virchow, constituted another historic example.

Dr. Allen O. Whipple had no peer as mentor to teach him how to resect a cancer at the head of the pancreas, so he reversed the system and sent his resident, Dr. Charles P. Mullins, to the research laboratory to devise the Whipple resection of the head of the pancreas with its cancer of the ampulla of Vater. With Mullins assisting at the first operation, the patient expired postoperatively from dissolution of the catgut sutures by the pancreatic juice. Mullins recommended 'to his mentee' that he should use nondigestible silk sutures and, thereafter, this proved successful.

*My advice:* Choose an established investigator who has an ongoing research program and who is interested in the mentee's research but also in the advancement of the mentee's career.

Today, if research of the pancreas is to include human resection, translocation or transplantation of the pancreas, a surgical mentor is obviously vital – for the history of pancreatic surgery clearly demonstrates the high mortality rate resulting from the 'occasional resector' of the pancreas. Thus, for any investigator undertaking research on patients, which may involve a life-threatening manipulation of the pancreas, mentoring by an experienced pancreatic surgeon is mandatory.

In the 1940s, pancreatic research laboratories were few and far between. Scores of research applicants sought fellowships in our laboratory and clinic. Planned experiments required expertise beyond my experience. The key was to provide a panel of mentors. Dr. Hubert Appert, PhD (Physiology), Dr. Fred Pairent, PhD (Chemistry), and other comparable scientists joined the young train-

ees and me in planning and initiating the experiments. Support by the National Institutes of Health was an important asset. The beginning research fellow was able to initiate and complete a preliminary investigation, which could be of his own design or part of a planned program. In such an environment I, as mentor, could simultaneously experience a lifelong career of continued growth, both as mentee and as mentor.

**M.E.F.-Z.:** What is the best advice you have received during your career?

**J.M.H.:** Keep at it! Accept the challenges of your critics. Your differences stem from variations of perspective. Ignore pettiness. It stems from jealousy.

**M.E.F.-Z.:** What is your advice to the young investigators that are beginning in the field of pancreatic research?

**J.M.H.:** To paraphrase Professor George Sarton of Princeton, 'We can measure our knowledge, we cannot measure our ignorance'.

Learn the fundamentals of molecular biology. It may well provide a greater avenue of advance than did the discovery of the microscope. Look also to the field of stem cell research.

**M.E.F.-Z.:** What do you think are the big questions that need to be answered in pancreatology?

**J.M.H.:** What is the specific mechanism whereby metastatic exocrine pancreatic cancer causes the death of a patient? How can it be blocked or otherwise treated? What is the cause of pancreatic cancer and how can it be prevented? Pertinent, but of lesser importance: Is the massive peripancreatic and retroperitoneal fat necrosis, sometimes associated with acute pancreatitis, due to enzymatic digestion or to ischemia?

**M.E.F.-Z.:** What do you think is the major need that a journal like *Pancreatology* should fill?

**J.M.H.:** The journal is currently first-class in its development of a multidisciplinary, international publication on pancreatology. This is a tough but wonderful journey. The journal might seek progress reports from involved investigators as to understanding the cause and possible routes to solution of the big problems – such as, why does metastatic cancer of the pancreas cause death? Does it produce a toxin? Does it cause a specific nutritional deficiency? Might such mentoring of the profession stimulate both clinical and laboratory investigation?